

# Single 1 g dose of cefotaxime in the treatment of infections due to penicillinase-producing strains of *Neisseria gonorrhoeae*

G A J DE KONING,\* D TIO,\* J A R VAN DEN HOEK,\* AND B VAN KLINGEREN†

From the \*Venereal Disease Clinics, Municipal Health Service, Amsterdam, and the †National Institute of Public Health, Bilthoven, The Netherlands

**SUMMARY** One hundred and two patients with an uncomplicated infection due to penicillinase-producing strains of *Neisseria gonorrhoeae* (PPNG) were treated with a single 1 g dose of cefotaxime. At follow-up within 15 days all genital and rectal infections were cured. Pharyngeal infections also seemed to respond to this treatment. A relatively high proportion (30·9%) of patients, however, developed post-gonococcal urethritis.

## Introduction

Since the prevalence of penicillinase-producing strains of *Neisseria gonorrhoeae* (PPNG) has increased, more effective treatment for this form of gonorrhoea has to be found. In Amsterdam prostitutes play a major role in spreading this disease.<sup>1</sup> Over the last few months in our laboratory 13·6% of all gonococcal strains produced penicillinase.

Cefotaxime is a third generation cephalosporin. The activity of the cephalosporin antibiotics against penicillinase-producing *N gonorrhoeae* is the result of good penetration of the cell wall, resistance of the antibiotic to bacterial  $\beta$ -lactamase, and combination with and inactivation of various penicillin-sensitive enzymes (penicillin-binding proteins) produced by the organism, some of which are essential to its metabolism and multiplication.<sup>2</sup> Hunter Handsfield<sup>3</sup> had a 93% success rate in treating patients with non-PPNG infections with a single dose of 1 g cefotaxime. The minimal inhibitory concentration of cefotaxime is the same for both non-penicillinase-producing and penicillinase-producing strains of gonorrhoea.<sup>4,5</sup> The peak plasma concentration after a 1 g dose of cefotaxime intramuscularly is 20·5  $\mu$ g/ml and the mean plasma half-life is 1·3 hours.<sup>6</sup>

In this study the efficacy of a single dose of cefotaxime in the treatment of uncomplicated urogenital, rectal, and pharyngeal infections due to PPNG strains was evaluated.

## Patients and methods

Only patients who had PPNG infections and who attended for review within 15 days of treatment were included in this study, which was carried out during 1981. Patients with a history of penicillin allergy, pelvic inflammatory disease, or disseminated gonorrhoea due to PPNG, pregnant women, and patients who had taken antibiotics in the previous 10 days were not included. A total of 102 patients (68 men and 34 women) were treated with a 1-g single dose of intramuscular cefotaxime diluted in 1% xylocaine to a volume of 4 ml.

## DIAGNOSIS

In addition to direct microscopy of Gram-stained smears of material from the urethra in men and the urethra and cervix in women, routine samples for culture were collected from the urethra and the throat in heterosexual men, from the urethra, the throat, and the rectum in homosexual men, and from the cervix, the throat, and the rectum in women. Specimens from the urethra and cervix were plated on chocolate agar plates (with 7% heated sheep blood). Samples from the throat, the rectum, and a second from the cervix were inoculated on to a modified Thayer-Martin medium (Oxoid). All cultures were confirmed as being *N gonorrhoeae* by colonial morphology, Gram-stain, oxidase test, and

Address for reprints: Dr G A J de Koning, VD Clinic, Municipal Health Service, Groenburgwal 44, 1011 HW Amsterdam, The Netherlands

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standard sugar utilisation patterns; penicillinase production was detected by the chromogenic cephalosporin test (Nitrocef, Glaxo). Patients were treated on the basis of positive microscopy and culture results.

#### DRUG SENSITIVITY

The susceptibility of the strains to antibiotics was determined at the National Institute of Public Health by the agar dilution technique using a multipoint inoculator. The antibiotics were incorporated into Isosensitest agar base (Oxoid) supplemented with 5% (v/v) horse blood. Among the antibiotics tested were cefotaxime and cefuroxime, since these cephalosporins are regarded as the drugs of first choice in the treatment of infections due to PPNG. The minimum inhibitory concentrations (MICs) of these drugs were determined for 99 of the PPNG isolates from the 102 patients.

#### FOLLOW-UP

The patients were asked to return for review between seven and 15 days after treatment. At the follow-up examination the same procedure was followed as at the first examination.

The male patients were investigated for post-gonococcal urethritis (PGU) by the examination of a urethral smear ( $\geq 10$  leucocytes/high-power field being regarded as positive).

#### Results

Of the 102 patients (68 men and 34 women) with PPNG infection treated with cefotaxime (1 g im), all were cured. The mean age (years)  $\pm$  standard deviation was  $31.1 \pm 6.7$  for the men,  $26.6 \pm 8.4$  for the women, and  $29.6 \pm 7.5$  for all patients.

The sites from which the PPNG strains were cultured in these patients are shown in table I. Of the 68 men with a urethral PPNG infection one had a

concomitant pharyngeal infection. One woman had a pharyngeal PPNG infection only and seven an anorectal infection; of these one had PPNG infection in the ano-rectum only. Of the 68 men, 21 (30.9%) developed a post-gonococcal urethritis. During treatment with cefotaxime only two patients spontaneously complained of side effects. One patient developed an erythematous macular rash two days after treatment and one complained of dizziness and nausea two hours after injection.

#### DRUG SENSITIVITIES

The distribution of the sensitivities of cefotaxime and cefuroxime are given in table II. The MICs for 99 of the isolates from the 102 patients were determined. In vitro cefotaxime is about 10 times as active as cefuroxime against PPNG strains, with 90% of the strains being inhibited by concentrations as low as  $0.004 \mu\text{g/ml}$ . Only one isolate had a decreased susceptibility to cefotaxime ( $\text{MIC} = 0.25 \mu\text{g/ml}$ ), but the patient was cured with the dosage given. The susceptibility testing was carried out within the framework of the national PPNG surveillance programme not only with the above cephalosporins but also with erythromycin, spectinomycin, tetracycline, and thiamphenicol. The results obtained with more than 900 PPNG strains isolated in 1981 have been reported.<sup>7</sup>

TABLE II Minimum inhibitory concentrations ( $\mu\text{g/ml}$ ) for 99 isolates of penicillinase-producing *N gonorrhoeae*

Antimicrobial agent	$\leq 0.004$	0.008	0.015	0.03	0.06	0.12	0.25
Cefotaxime	90	5	1	2	12		1
Cefuroxime			18	63	12	2	4

#### Discussion

Hunter Handsfield<sup>3</sup> showed that 93% of 55 patients with non-PPNG infections treated with cefotaxime were cured. Nayyar<sup>8</sup> had a high success rate (98.8%) in patients infected with both PPNG and non-PPNG strains treated with another second generation cephalosporin, cefuroxime. This study shows that cefotaxime (Claforan) was a painless, safe, and highly effective (100%) treatment for genital and rectal PPNG infections. The three cases of pharyngeal PPNG infection seemed to be cured, although only one follow-up culture was performed.

One disadvantage of this treatment, as with ampicillin, penicillin, and cefuroxime, is the high incidence of PGU (30.9%) in male patients. In our

TABLE I Sites from which penicillinase-producing *N gonorrhoeae* (PPNG) strains were isolated

Sites	No of patients infected with PPNG:		
	Men	Women	Total
Urethra	67	1	68
Anorectum		1	1
Cervix		9	9
Pharynx		1	1
Urethra + pharynx	1		1
Urethra + cervix + anorectum		5	5
Cervix + urethra		15	15
Cervix + anorectum		1	1
Cervix + pharynx		1	1
Total	68	34	102

study cefotaxime was 10 times as active in vitro as cefuroxime, and only one isolate had a decreased susceptibility to cefotaxime. Nevertheless, the warning of Boakes<sup>9</sup> should be heeded that "the development of wide spread resistance to  $\beta$ -lactamase stable antibiotics is a fearsome prospect and may be encouraged if these drugs are used for the routine treatment of gonorrhoea instead of being reserved for known or strongly suspected penicillin resistant infections." In Amsterdam prostitutes play an important role in the spread of PPNG infection. Since January 1981 prostitutes and their clients have been regarded as at high risk of PPNG infection and they are treated routinely with cefotaxime.

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